CLAIMS

We Claim:

1. A nucleic acid molecule encoding a fusion protein which comprises

(a) an effector module which is intracellularly cytotoxic, the effector module comprising one of the mistletoe lectin A chain, a fragment thereof, and a derivative thereof, wherein the mistletoe lectin A chain is encoded by a nucleic acid molecule selected from the group consisting of:

(i) a nucleic acid molecule which has a nucleotide sequence encoding at least a fragment of a protein having the amino acid sequence SEQ ID NO: 2;

(ii) a nucleic acid molecule having the nucleotide sequence of at least a fragment of SEQ ID NO: 1;

(iii) a nucleic acid molecule which hybridizes with the nucleic acid molecule of (i) or (ii); and

(iv) a nucleic acid molecule which is degenerate with respect to the nucleic acid molecule of (iii);

(b) a processing module which is covalently linked to the effector module and which comprises a recognition sequence for a protease, wherein the processing module comprises one of the mistletoe lectin propeptide, a fragment thereof, and a derivative thereof, and wherein the mistletoe lectin propeptide is encoded by a nucleic acid molecule selected from the group consisting of:

(i) a nucleic acid molecule which has a nucleotide sequence encoding at least a fragment of a protein having the amino acid sequence SEQ ID NO: 6;

(ii) a nucleic acid molecule having the nucleotide sequence of at least a fragment of SEQ ID NO: 5;

(iii) a nucleic acid molecule which hybridizes with the nucleic acid molecule of (i) or (ii); and

(iv) a nucleic acid molecule which is degenerate with respect to the nucleic acid molecule of (iii); and

(c) a targeting module which is covalently linked to the processing module and which specifically binds to the surface of a cell, thereby mediating internalization of the fusion protein into the cell.

2. The nucleic acid molecule of claim 1, wherein the effector module possesses the biological activity of the mistletoe lectin A chain and has at least one amino acid deletion, substitution, insertion, addition, or exchange with respect to the mistletoe lectin A chain.

3. The nucleic acid molecule according to any of claim 1, wherein the processing module is proteolytically cleavable and has at least one amino acid deletion, substitution, insertion, addition, or exchange with respect to the mistletoe lectin propeptide.

4. The nucleic acid molecule of claim 1, wherein the fusion protein further comprises a modulator module which is covalently linked to one of the processing module, the effector module, and the targeting module, and wherein the modulator module modulates the intracellular cytotoxicity of the effector module.

5. The nucleic acid molecule of claim 4, wherein the modulator module is encoded by a nucleic acid molecule selected from the group consisting of:

(i) a nucleic acid molecule having a nucleotide sequence which encodes at least a fragment of a protein having the amino acid sequence SEQ ID NO: 4;

(ii) a nucleic acid molecule which has the nucleotide sequence of at least a fragment of SEQ ID NO: 3;

(iii) a nucleic acid molecule which hybridizes with the nucleic acid molecule of (i) or (ii): and

(iv) a nucleic acid molecule which is degenerate with respect to the nucleic acid molecule of (iii).

6. The nucleic acid molecule of claim 5, wherein the modulator module possesses the biological activity of the mistletoe lectin B chain and has at least one amino acid deletion, substitution, insertion, addition, or exchange with respect to the mistletoe lectin B chain.

7. The nucleic acid molecule of claim 4, wherein the fusion protein further comprises an affinity module which is covalently linked to one of the effector module, the processing module, the targeting module, and the modulator module.

8. The nucleic acid molecule of claim 1, wherein the processing module is of plant origin and has an amino acid sequence selected from the group consisting of

(i) the sequence SSSEVRYWPLVIRPVIA and

(ii) the sequence S4-S3-S2-S1/-S1', wherein S1 is one of an arginine residue and a lysine residue, S2 is an amino acid residue selected from the group consisting of phenylalanine, tyrosine, valine, and leucine, and neither S3 nor S4 is proline.

9. The nucleic acid molecule of claim 1, wherein the targeting module specifically recognizes a cell selected from the group consisting of the immune system, a tumor cell, and a cell of the nervous system.

10. The nucleic acid molecule of claim 9, wherein the cell of the immune system is a cell of the specific immune system

11. The nucleic acid molecule of claim 10, wherein the cell of the specific immune system is a T cell

12. The nucleic acid molecule of claim 11, wherein the T cell is a T_H2 cell.

13. The nucleic acid molecule of claim 9, wherein the cell of the immune system is a cell of the unspecific immune system

14. The nucleic acid molecule of claim 9, wherein the tumor cell is a degenerate cell of the immune system.

15. The nucleic acid molecule of claim 1, wherein the affinity module comprises a portion selected from the group consisting of a histidine sequence, thioredoxin, strep-Tag, T7-Tag, Flag-Tag, maltose-binding protein, and GFP.

16. The nucleic acid molecule of claim 1, wherein the modulator module has a portion comprising one of the mistletoe lectin B chain, a fragment thereof, a derivative thereof, the peptide KDEL, and the peptide HDEL.

17. The nucleic acid molecule of claim 16, wherein the mistletoe lectin B chain has at least one amino acid exchange at an amino acid position selected from the group consisting of positions 23, 38, 68, 70, 75, 79, 235, and 249.

18. The nucleic acid molecule of claim 17, wherein the exchange is selected from the group consisting of substitution of A at position D23, substitution of A at position W38, substitution of A at position D235, substitution of A at position Y249, substitution of S at position Y68, substitution of S at position Y70, substitution of S at position Y75, and substitution of S at position F79.

19. The nucleic acid molecule of claim 1, wherein the is nucleic acid molecule is DNA.

20. The nucleic acid molecule of claim 1, wherein the is nucleic acid molecule is RNA.

21. A vector comprising a nucleic acid molecule of claim 1.

22. A host which is transformed with a vector of claim 21

23. The host of claim 22, wherein the host is a prokaryote.

24. The host of claim 23, wherein the prokaryote is selected from the group consisting of *E. coli*, *Bacillus subtilis*, and *Streptomyces coelicolor*.

25. The host of claim 22, wherein the host is a eukaryote.

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26. The host of claim 25, wherein the eukaryote is selected from the group consisting of a *Saccharomyces* sp., an *Aspergillus* sp., a *Spodoptera* sp., and *Pichia pastoris*.

27. A host which comprises a nucleic acid molecule of claim 1.

28. A fusion protein which is produced by a host of claim 27.

29. A process for producing a fusion protein, the method comprising culturing a host of claim 27 and isolating the fusion protein from the host.

30. A fusion protein which is encoded by the nucleic acid molecule of claim 1.

31. A medicament comprising a fusion protein of claim 30 and a pharmaceutically acceptable carrier.

32. A medicament comprising (a) one of

(i) a fusion protein encoded by a nucleic acid molecule of claim 1

and

(ii) a vector which comprises the nucleic acid molecule of (i);

and (b) one of

(iii) a modulator module which is covalently linked to one of a processing module and an effector module, wherein the modulator module modulates the intracellular cytotoxicity of the effector module

and

(iv) a vector which comprises a nucleic acid encoding the modulator module of (iii).

33. A kit, comprising at least one of

(a) a vector which comprises a nucleic acid molecule of claim 1; and

(b) a vector which comprises a nucleic acid molecule of claim 1;

and a vector which comprises a nucleic acid molecule encoding a modulator which modulates the intracellular cytotoxicity of the effector module of (a) and/or (b).

34. A nucleic acid molecule encoding a fusion protein which comprises

(a) an effector module which is intracellularly cytotoxic, the effector module comprising one of the mistletoe lectin A chain, a fragment thereof, and a derivative

thereof, wherein the mistletoe lectin A chain is encoded by a nucleic acid molecule selected from the group consisting of:

(i) a nucleic acid molecules which has a nucleotide sequence encoding at least a fragment of a protein having the amino acid sequence SEQ ID NO: 2;

(ii) a nucleic acid molecule which has the nucleotide sequence of at least a fragment of SEQ ID NO: 1;

(iii) a nucleic acid molecule which hybridizes with the nucleic acid molecule of (i) or (ii); and

(iv) a nucleic acid molecule which is degenerate with respect to the nucleic acid molecule of (iii);

(b) a processing module which is covalently linked to the effector module and which comprises a recognition sequence for a protease; and

(c) a targeting module which is covalently linked to the processing module and which specifically binds to the surface of a cell, thereby mediating internalization of the fusion protein into the cell.

35. The nucleic acid molecule of claim 34, wherein the processing module comprises one of the mistletoe lectin propeptide, a fragment thereof, and a derivative thereof.

36. A nucleic acid molecule encoding a fusion protein which comprises

(a) an effector module which is intracellularly cytotoxic;

(b) a processing module which is covalently linked to the effector module and which comprises a recognition sequence for a protease, wherein the processing module comprises one of the mistletoe lectin propeptide, a fragment thereof, and a derivative thereof, and wherein the mistletoe lectin propeptide is encoded by a nucleic acid molecule selected from the group consisting of:

(i) a nucleic acid molecule which has a nucleotide sequence encoding at least a fragment of a protein having the amino acid sequence SEQ ID NO: 6;

(ii) a nucleic acid molecule which has the nucleotide sequence of at least a fragment of SEQ ID NO: 5;

(iii) a nucleic acid molecule which hybridizes with the nucleic acid molecule of (i) or (ii); and

(iv) a nucleic acid molecule which is degenerate with respect to the nucleic acid molecules mentioned in (iii); and

(c) a targeting module which is covalently linked to the processing module and which specifically binds to the surface of a cell, thereby mediating internalization of the fusion protein into the cell.

37. The nucleic acid molecule of claim 36, wherein the effector module comprises one of the mistletoe lectin A chain, a fragment thereof, and a derivative thereof.

38. A method of modulating the effect of an intracellularly active toxin, the method comprising providing one of a mistletoe lectin B chain, a fragment thereof, and a derivative thereof to the interior of a cell and intracellularly cleaving a fusion protein comprising

(a) an effector module which comprises the toxin;

(b) a processing module which is covalently linked to the effector module and which comprises a recognition sequence for a protease; and

(c) a targeting module which is covalently linked to the processing module and which specifically binds to the surface of a cell, thereby mediating internalization of the fusion protein into the cell.

39. The method of claim 38, wherein the fusion protein further comprises

(e) an affinity module which is covalently linked to one of the effector module, the processing module, the targeting module, and the modulator module.

40. The method of claim 38, wherein the toxin is selected from the group consisting of the A chain of a type II RIP, and the A chain of a type I RIP, an intracellularly toxic fragment of a type II RIP, an intracellularly toxic fragment of a type I RIP, a derivative of a type II RIP, and a derivative of a type I RIP.

41. The method of claim 40, wherein the type II RIP is selected from the group consisting of ricin, mistletoe lectin, abrin, ebulin, modeccin, and volkesin.

42. The method of claim 40, wherein the type I RIP is selected from the group consisting of saporin, gelonin, agrostin, asparin, bryodin, colocin, crotin, curzin, dianthin, luffin, trichosanthin, and trichokirin.

43. A process for testing a prospective modulator *in vitro*, the method comprising

(a) transfecting a target cell with a vector which comprises a nucleic acid molecule of claim 1;

(b) transfecting the target cell with a vector which contains a nucleic acid encoding a prospective modulator;

(c) expressing the nucleic acids in the target cell; and

(d) measuring the modulating activity of the prospective modulator on the toxicity of the toxin.

44. A process for testing a prospective modulator *in vitro*, the method comprising

(a) transfecting a target cell which contains a nucleic acid molecule of claim 1 with a vector which comprises a nucleic acid encoding the prospective modulator;

(b) expressing the nucleic acids in the target cell; and

(c) measuring the modulating activity of the prospective modulator on the toxicity of the toxin.

45. A method of producing a prospective modulator, the method comprising

(a) transfecting a target cell with a vector which comprises a nucleic acid molecule of claim 1;

(b) transfecting the target cell with a vector which comprises a nucleic acid encoding the prospective modulator;

(c) expressing the nucleic acids in the target cell;

(d) measuring the modulating activity of the prospective modulator on the toxicity of the toxin; and

(e) isolating the modulator.

46. A method of producing a prospective modulator, the method comprising

(a) transfecting a target cell which contains a nucleic acid molecule of claim 1 with a vector which comprises a nucleic acid encoding the prospective modulator;

(b) expressing the nucleic acids in the target cell;

(c) measuring the modulating activity of the prospective modulator on the toxicity of the toxin; and

(d) isolating the modulator.